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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Roy A. Gravel *et al.*	Art Unit:	Not yet assigned
Serial No.:	Not yet assigned	Examiner:	Not yet assigned
Filed:	June 27, 2003	Customer No.	21559

Title: HUMAN METHIONINE SYNTHASE: CLONING, AND METHODS FOR EVALUATING RISK OF NEURAL TUBE DEFECTS, CARDIOVASCULAR DISEASE, AND CANCER

Mail Stop Patent Application
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Version with Markings to Show Changes Made

A marked-up version of the first paragraph of the specification is shown below.

This application is a continuation of pending US Application Number 08/980,326, filed November 26, 1997, which claims the benefit of U.S. Provisional Application No. 60/031,964, filed November 27, 1996, and Provisional Application No. 60/050,310, filed June 20, 1997. [This invention claims priority from U.S. Provisional Applications Serial Nos. 60/031,964 and 60/050,310, filed November 27, 1996 and June 20, 1997, respectively].

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U.S. Provisional Application No. 60/031,964, filed November 27, 1996, and Provisional Application No. 60/050,310, filed June 20, 1997.

REMARKS

As presently claimed, the invention provides methionine synthase nucleic acids and kits containing them.

The present claims represent amended versions of claims 3, 4, 6, 26, 34-37, and 40 from parent application U.S.S.N. 08/980,326, and are believed to be in condition for allowance. Specifically, in the Office Action received in connection with this parent application (mailed April 9, 2003; "Office Action"), a written description rejection under 35 U.S.C. § 112 and novelty rejections under 35 U.S.C. §102(a) and (b) were raised. These rejections are addressed below.

Support for Pending Claims

The pending claims find support throughout the specification, for example, pages 4-6, 10-12, 24, and 35. These claims contain no new matter.

Written Description Rejection from Parent Case

Regarding the written description rejection, the Office Action stated that the specification failed to convey possession of the invention of prior claims 4, 6, 26, 34, 36, 37, and 40.

In particular, the Office stated that the specification provides one species of mammalian methionine synthase nucleic acids (i.e., human methionine synthase) and does not provide nucleic acids from other species covered by prior claims 4, 36, and 37. As currently drafted, the corresponding claims (claims 2, 7, and 8) specify that the nucleic acid is a *human* nucleic acid. Applicants note that this amendment has been made in the interest of expediting prosecution, and applicants reserve the right to pursue the original or related claims in this or a future, related application. Applicants further note that the specification clearly discloses

important structural features of the claimed human methionine synthase nucleic acids. In particular, all methionine synthase genes known at the time of filing, share exceptionally high sequence identity to *four discreet regions* (Boxes 1-4, such as the cobalamin binding domain illustrated in Fig. 1 of the specification) of the encoded polypeptide. Indeed, the human methionine synthase gene was isolated due to the high homology to these four box/regions. Thus, applicants' teachings of these four highly conserved domains of human methionine synthase, the complete cDNA sequence of human methionine synthase, and three mutant forms of human methionine synthase satisfy the written description requirement set forth by the case law and the U.S. Patent & Trademark Office's Written Description Guidelines (the "Guidelines").

The Guidelines, under the "Genus Analysis" decision tree, states:

> What is a representative number of species depends on whether one of skill in the art would recognize that applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed or claimed. (Emphasis added.)

Given that applicants' specification describes the claimed class of human methionine synthase nucleic acids and their shared, characteristic domains, this standard is satisfied, and claims 2, 7, and 8 should be allowed.

The Office also asserted that the specification does not describe kits directed to mutations other than the three mutations described in the specification. Present claims 3, 9, and 10 (which correspond to prior claims 6, 26, and 40 from the parent case) specify that the mutation or polymorphism is D919G, H920D, or ΔIle881. In view of this amendment, claims 3, 9, and 10 should be allowed.

Novelty Rejections from Parent Case

Prior claims 3, 4, 6, 34-37, and 40 were rejected, under 35 U.S.C. § 102(a), as being anticipated by Marra *et al.* (GenBank Accession No. W33307), and prior

claims 3, 4, and 37 were further rejected, under 35 U.S.C. § 102(b), as being anticipated by Bannerjee *et al.* (GenBank Accession No. J04975). Marra and Bannerjee disclose murine and bacteria sequences, respectfully. As currently drafted, the corresponding present claims (claims 1-8 and 10) recite human nucleic acids and thus are free of these rejections.

CONCLUSION

Applicants submit that this application is in condition for allowance, and such action is respectfully requested.

If there are any charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: June 27, 2003

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